66. (Amended)   A method of claim 53, wherein the APP substrate comprises a human APP isoform and the determining step comprises measuring the production of amyloid alpha peptide (sAPPα).

67. (Amended)   A method of claim 53, wherein the method further comprises steps of:

(c)   determining the level of hu-Asp1 α-secretase activity in the presence and absence of a modulator of hu-Asp1 α-secretase activity; and

(d)   comparing the hu-Asp1 α-secretase activity in the presence and absence of the modulator, wherein modulators that increase hu-Asp1 α-secretase activity are identified as candidate Alzheimer's disease therapeutics.

68. (Amended)   A method of claim 67, wherein the method further comprises a step of treating Alzheimer's Disease with said candidate Alzheimer's disease therapeutic.

70. (amended)   The substrate of claim 69, wherein the substrate comprises a detectable label.

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